REMARKS

Status of Claims

Prior to entry of this paper, claims 1-3, 5-8, 10-11, 14-15, 17-19, 21-24, 27-30, and 33-41 were pending and subject to restriction.

Claim 2 is canceled herein. Claims 1, 3, 5-8, 10-11, 14-15, 17-19, 21-24, 27-29, 33-36, 38, and 40 are amended herein. New claims 42-100 are presented herein. No new matter is introduced.

Upon entry of this paper, claims 1-3, 5-8, 10-11, 14-15, 17-19, 21-24, 27-30, and 33-100 are pending. Applicants reserve the right to pursue any canceled subject matter in one or more continuing applications.

Support for Amendments

Claim 1 is amended to delete reference to collagen. Support can be found in the specification as filed, for example at page 6, lines 1-14. Claim 1 is also amended to specify that the HA or derivative thereof comprises at least 10% (w/w) of the haemostatic composition. Support can be found in the specification as filed, for example at page 8, lines 14-15.

Claim 5 is amended to be directed to an embodiment of the invention having at most 90% (w/w) gelatin. Support can be found in the specification as filed, for example at page 8, lines 22-30.

Claims 3, 27, 29, 33, 35, 36, 38, and 40 are amended to remove typographical errors, correct dependency, present the phrase "hyaluronic acid (HA)" consistently, or present a claim in independent form.

Claims 1, 3, 5, 6, 7, 8, 10, 11, 14, 15, 17, 18, 19, 21, 22 are amended to cite a "composition" rather than "sponge, powder or flakes". Support can be found in the specification as filed, for example at page 5, lines 1 to 3.

New claims 42-100 are directed to various embodiments of the invention. Support can be found throughout the specification as filed, for example at page 4, lines 15-30, at page 7, lines 1-12, at page 19, lines 34-39, at pages 26-27 (Examples 1-3), and at page 8, lines 22-30. Support for exclusion of collagen can be found throughout the specification as filed, for example at page 1, line 5, page 22, line 6, and page 23, line 36 which describe gelatin as a preferred biologically absorbable material. In addition, on page 5, line 31 to page 6, line 21, the degradation, origin, and stabilization of gelatin are discussed.

Support for additional embodiments can be found as follows. Claims 60-61, directed to different methods for cross-linking hyaluronic acid, find support on page 7, line 14. Claim 62, directed to the pH value of the hyaluronic acid, finds support on page 7, lines 14-17. Claim 63, directed to hyaluronic acid derivatives, finds support on page 7, line 21 through page 8, line 7. Claim 64, directed to buffering agents, finds support on page 12, lines 30-34. Claims 65-78, directed to various anti-microbial agents, find support on page 13, line 31 through page 14, line 6. Claim 79, directed to various agents, finds support on page 13, lines 9-30. Claims 80-84, directed to various surfactants, find support on page 14, lines 8-32. Claim 85, directed to preservatives, finds support on page 14, lines 34-37.

In summary, support for the amendments can be found in the specification and claims as originally filed. No new matter is introduced.

Restriction Requirement

The pending claims have been restricted into Group I (claims 1-3, 5-8, 10, 11, 14, 15, 17, 18, and 40), drawn to a haemostatic composition; Group II (claims 19, 21-24, and 41), drawn to a method of using the haemostatic composition, and Group III (claims 27-30, 33-39, and 41), drawn to a method of making the haemostatic composition.

Applicants elect Group I (claims 1-3, 5-8, 10, 11, 14, 15, 17, 18, and 40, drawn to a haemostatic composition) with traverse. Applicants believe new claims 42-100, directed to a haemostatic composition, should be examined with Group I.

The traversal is on the basis that, contrary to the Examiner's contention, the pending claims share a special technical feature. In particular, the cited Yannas (US Patent No. 4,280,954) reference fails to teach haemostatic compositions comprising gelatin and HA or derivative thereof, where the amount of HA or derivative thereof is at least 10% (w/w), or by teaching a haemostatic composition comprising gelatin and HA or a derivative thereof, wherein the HA or derivative thereof is incorporated into the composition by cross-linking with dry heat at 110-200°C, or by teaching an HA or derivative thereof having a molecular weight of from 1,500 to 5,000 kDa. In other words, Yannas fails to destroy the novelty of the pending claims, and therefore the pending claims define a special technical feature over Yannas.

Applicants submit that not only does Yannas fail to destroy the unity of the present claims, but also that Yannas is not relevant to the patentability of the amended claims, as described below.

Yannas teaches composite materials of collagen and a mucopolysaccharide which are said to have anti-coagulant properties. In addition, the cross-linked mucopolysaccharides of Yannas serve to improve stability *in vivo* with increased resistance to resorption while

maintaining blood compatibility (see Yannas, col. 3, lines 12-13, 21-25, and 31-33). In contrast, the instant compositions comprise gelatin and they are pro-coagulant. Therefore, the invention is directed to solving a different technical problem than Yannas.

Moreover, Yannas teaches seven different species of mucopolysaccharide and notes differences between HA and the other species with respect to performance. For example, Example 15 of Yannas provides results of a resorption resistance assay. The assay shows that while all other composite materials exhibit reduced collagen degradation, material with collagen cross-linked to HA fails to exhibit this property (see column 25, Table IX and lines 57-65). Furthermore, Examples 12 and 13 of Yannas show that the HA-collagen composites fail to exhibit significant differences in whole blood clotting time (WBCT) compared to collagen itself. These data demonstrate that collagen-HA is comparable to collagen alone in reducing whole blood clotting time under the conditions specified by Yannas, and therefore would not suggest the use of this combination in a pro-clotting combination. Indeed, the data presented by Yannas highlight the surprising discovery that compositions comprising gelatin and HA according to the present invention possess a pro-coagulant effect.

Even more surprising is the synergy shown by the components of the present invention. For instance, Example 6 of the present application show that gelatin sponges with HA reduce bleeding intensity more than gelatin sponges without HA. A gelatin sponge with 30% HA reduces bleeding 5.2 times better than a gelatin sponge without HA (Table on page 32, S4 versus S1). Collagen in combination with 10% HA also reduces bleeding, i.e., 1.43 times better than collagen alone (see page 32, lines 8-13 of the present application). While not wishing to be bound by theory, the lower amount of incorporated HA may account for some of the effect, which is supported by data in Example 6 of the present application, i.e., gelatin powder with 10%

HA reduces bleeding 1.28 times better than gelatin powder alone, while the gelatin sponge with 30% HA reduces bleeding 5.2 times better than the gelatin sponge without HA, as noted above.

On the other hand, the examples of Yannas have a percentage of HA in the composite materials ranging from 2.3% $\pm$ 0.5 to 9.0% $\pm$ 0.5. In contrast, the present application discloses compositions of at least 10% (page 8, lines 9-20), with examples of specific use of HA in amounts of at least 13% (Example 3), 25-50% (Example 1) and 30% (Examples 6 and 7). For at least the reason that Yannas provides examples with a lower amount of HA which yield a different effect, Yannas does not preclude a special technical feature for the instant claims. Moreover, the examples of Yannas have a maximum of 9.5% HA in combination with collagen, so it could not have been predicted from Yannas that the incorporation of 10% or more HA into a gelatin-based composition would have a synergistic effect on haemostasis, as described above.

Furthermore, Yannas fails to teach a composition as instantly claimed, but rather discloses anti-coagulant materials such as films, tape, membranes and composites. Applicants note that when a sponge is claimed, the instant specification provides a definition of a sponge on page 5, lines 13-18, as a porous structure that may absorb liquid. This is in contrast to the grafts or implants taught by Yannas, which are not intended to absorb liquid. Yannas does not disclose sponge structures, as the collagen-HA of Yannas loses weight due to degradation, and the other composites initially de-swell upon implantation.

Finally, Applicants note that Yannas describes HA derived from rooster comb, employing the method of Swann et al. for extraction. Swann et al. states that HA is a polydisperse product with both high and low molecular weight species, but Swann actually provides a molecular weight of 230 to 1,200 kDa for the different HA fractions (see Swann, page 24, Table III). For comparison, the molecular weight range cited e.g. in claim 45 is from 1,500 to

5,000 kDa. It is also worth noting that Yannas teaches physical cross-linking, but only with temperatures of up to 95°C (see col. 9, lines 2-28). In contrast, e.g. claims 23, 24, 33, 40, 42 and 43 of the present application cite that – surprisingly – it is possible to use cross-linking with dry heat at higher temperatures than Yannas, namely 110-200°C (see e.g. page 18, line 27).

In view of the substantial differences between Yannas and the instant claims, Applicants respectfully request withdrawal of the restriction requirement for failure to provide a special technical feature over Yannas and allowance of the application.

CONCLUSION

Applicants respectfully submit that the instant application is in condition for allowance. In the event that a telephone conference would facilitate examination of this application in any way, the Examiner is invited to contact the undersigned at the number provided.

AUTHORIZATION

The Commissioner is hereby authorized to charge any fees which may be required for this amendment, or credit any overpayment to Deposit Account No. **50-3732**, Order No. **13323.105005**. Furthermore, in the event that an extension of time is required, the Commissioner is requested to grant a petition for that extension of time which is required to make this response timely and is hereby authorized to charge any fee for such an extension of time or credit any overpayment for an extension of time to the above-noted Deposit Account No. **50-3732** and Order No. **13323.105005**.

Respectfully submitted,
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